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10/061,201	01/30/2002	Mark Shannon	PB0178	2093

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/061,201	SHANNON, MARK	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *7,13-31,34-38 and 40-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12,32,33 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 7/28/04. Claims 1-47 are currently pending in the application and are addressed herein.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-6, 8-12, 32, 33, 39) in the reply filed on 7/28/04 is acknowledged.

Claims 7, 13-31, 34-38 and 40-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/28/04.

Claims 1-6, 8-12, 32, 33, 39 are examined herein.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. For example, see page 6, line 25; page 19, line 22; page 73, line 10; page 74, line 26; page 76, line 19, etc. Correction of all embedded hyperlinks is required.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2).

However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 because Figure 1 contains sequences which must be identified using a proper sequence identifier (SEQ ID NO). Specifically, see Figure 1B-E (discloses many different sequences); however, the sequences have not been assigned appropriate SEQ ID NOS. Note that the sequence identifiers for the sequences in the figures must be disclosed either in the figures themselves or in the description of the figures in the specification. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) in response to this Office Action. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g).

Miscellaneous

In the instant case, the claims encompass nucleic acids that encode a POSH-like oncoprotein (POSHL1), including degenerate variants thereof and fragments or probes that would hybridize to the degenerate variant POSHL1 nucleic acids. It is noted that claim 1 explicitly claims "a degenerate variant of the sequences set forth in [SEQ ID NO: 2]". Looking to the specification for guidance with respect to the definition of "degenerate variants" it is noted that the specification discloses,

> "As used herein, the phrase 'degenerate variant' of a reference nucleic acid sequence intends all nucleic acid sequences that can be directly translated, using the standard genetic code, to provide an amino acid sequence identical to that translated from the reference nucleic acid sequence." (See page 10, lines 16-20).

As such, considering Merriam-Webster's Collegiate Dictionary defines "intends" as, "signify", "mean"; the phrase "degenerate variant" with respect to a nucleic acid encoding POSHL1 is interpreted as any nucleic acid sequence that, based on the genetic code, encodes the

disclosed amino acid sequence of POSHL1. Since the specification discloses SEQ ID NO: 2 as the amino acid sequence of human POSHL1, a "degenerate variant" of a nucleic acid sequence encoding POSHL1 encompasses only those nucleic acids which encode the amino acid sequence of SEQ ID NO: 2. Given this interpretation, the specification has disclosed an adequate written description of the "degenerate variants" encompassed by the claims.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8-12, 32, 33 and 39 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or, alternatively, a well-established utility.

The pending claims have been reviewed in light of the Revised Interim Utility Examination Guidelines and the Revised Interim Written Description Guidelines Training Materials.

The examiner is using the following definitions in evaluating the claims for utility.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's

assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

The instant claims are drawn to an isolated nucleic acid that encodes a POSH-like oncoprotein (POSHL1), including degenerate variants thereof, probes specific for said nucleic acid, a vector comprising said nucleic acid, a host cell transformed with said nucleic acid, and compositions comprising said nucleic acid wherein said compositions are designated "diagnostic" and "pharmaceutical" compositions. Since all claims encompass, to some extent, an isolated nucleic acid encoding a POSH-like oncoprotein, the utility for all claims require that the isolated nucleic acid encoding the POSH-like protein has utility. With respect to the probes, since the probes are only disclosed as useful for hybridizing to (and thus identifying in a sample) a nucleic acid encoding POSH-like protein, the nucleic acid encoding the POSH-like must have utility in order for the claimed probe to have utility.

Looking to the specification for an assertion of a credible, specific and substantial utility, for the claimed invention, it is noted that the specification asserts the following about the claimed isolated nucleic acids:

> "[T]he present inventors have identified human POSHL1, a proto-oncogene/oncogene product that functions as an adaptor protein that interacts with Rho family small GTpases as well as downstream components of the signal transduction pathway...
>
> [T]he newly isolated gene product shares certain protein domains and an overall structural organization with mouse POSH protein. **The shared structural features strongly imply that human POSHL1 plays a role similar to that of mouse POSH protein** in interacting with members of the Rho family small GTpases, as well as components of the JNK kinase cascade. **POSHL1 is a potential proto-oncogene/oncogene**...
>
> Like mouse POSH protein, human POSHL1 has one N-terminal RING finger domain and several SH3 domains (three SH3 domains for POSHL1 and four for POSH)... E3 ubiquitin-protein ligase activity is intrinsic to the RING finger domain of c-cbl and is likely to be a general function of this domain. Various RING finger domains exhibit binding activity towards E2 ubiquitin-conjugating enzymes (Ubc' s). SH3 (Src homology 3) domains are often indicative of a protein involved in signal transduction related to cytoskeletal organization. SH3 domain was first described in the Src cytoplasmic tyrosine kinase. The structure of SH3 is a partly opened beta barrel."
>
> (See page 6, line 6 through page 7, line 2 of the specification, emphasis added).

Therefore, applicants have asserted that the claimed invention has utility because human POSHL1 is a proto-oncogene/oncogene product that functions as an adaptor protein that interacts with Rho family small GTpases as well as downstream components of the signal transduction pathway. This is accepted as a credible utility.

However, with respect to the asserted utility as it applies to a specific and substantial utility, it is noted that there are many proto-oncogenes/oncogenes that are known in the prior art. However, the known genus of proto-oncogenes/oncogenes encompass molecules that are structurally and functionally different. Considering that proto-oncogenes/oncogenes encompass

a genus of molecules that have different chemical structures (i.e., different sequences) that function by different mechanisms to cause oncogenesis (e.g., they may utilize different signal transduction pathways), it is required that the activity that is specific for POSHL1 be disclosed. Since applicants have merely asserted that the claimed invention has utility as a proto-oncogene/oncogene without asserting any activity that is specific for POSHL1, the asserted utility is not a specific utility. It is noted, that the specification has based the asserted utility on the basis of the sequence homology of human POSHL1 with mouse POSH. The sequence homology analysis indicates that human POSHL1 may contain some of the domains that are present in mouse POSH. However, it is clear that the human POSHL1 and mouse POSH do not comprise identical domain structure (i.e., they differ in number of certain domains). Furthermore, the specification discloses that POSHL1 functions as an adaptor protein that interacts with Rho family small GTpases as well as downstream components of the signal transduction pathway. However, it is noted that are many different types of GTPases known in the prior art, including GTPases which have divergent functions in the cell. Additionally, the specification discloses that POSHL1 interacts with "downstream components of the signal transduction pathway". It is noted that there are thousands of different signal transduction pathways known in the cells, including pathways that use different downstream components, yet the specification has not identified which downstream components of which signal transduction pathway specifically interacts with POSHL1. That is, there is no data presented which indicates that POSHL1 specifically interacts with any specific GTPase or any specific downstream component of a signal transduction pathway. All of the asserted utilities are based solely on the sequence similarity of human POSHL1 to mouse POSH. It is also noted that the specification

acknowledges that the actual function of human POSHL1 has not been determined by stating, "The shared structural features strongly imply that human POSHL1 plays a role similar to that of mouse POSH protein in interacting with members of the Rho family small GTpases, as well as components of the JNK kinase cascade. POSHL1 is a potential proto-oncogene/oncogene..." (See p. 6, lines 12-19).

As indicated above, a substantial utility is one that has "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant case, there is no "real world" utility for the claimed invention because additional experimentation is required in order to first establish that human POSHL1 interacts with specific Rho GTPases and specific downstream components of the signal transduction pathway such that the function of POSHL1 in oncogenesis was clear. Furthermore, there are no asserted utilities found in the specification that would constitute a "real world" use for human POSHL1 without performing additional experimentation. As such, the claimed invention does not have substantial utility.

The last consideration is whether or not the there is a well-established utility that is specific, substantial and credible. A well-established utility may be found in the prior art, the specification or may be readily apparent to one of skill in the art. In the instant case, there is no well-established utility that is credible, specific and substantial found for the claimed isolated nucleic acid(s) encoding a POSH-like protein.

Additionally, claims 1-6, 8-12, 32, 33 and 39 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and

substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In addition to the 101 rejection above, claims 1-6, 8-12, 32, 33 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant rejection is set forth with respect the claims encompassing nucleic acids encoding a polypeptide having "conservative amino acid substitutions" (e.g., see claim 1, part (b)(ii)).

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The instant claims encompass nucleic acids that encode the polypeptide of SEQ ID NO: 2 wherein the polypeptide can comprise ANY conservative amino acid substitution. It is noted that the claim does not limit the number of substitutions; as such, the claims encompass a nucleic acid encoding the polypeptide of SEQ ID NO: 2 wherein all amino acids are conservative amino acid substitutions.

However, it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Attwood (Science, 290:471-473, 2000); Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual evidence is absent here. Therefore, the instant claims are enabled only the extent that they read on a polynucleotide encoding the polypeptide

polypeptide set forth in SEQ ID NO: 2. Considering that the claims encompass thousands of different polypeptides, additional experimentation would be required to determine which conservative amino acid substitutions retained the biological activity of POSHL1.

Conclusion

No claims is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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